# Stereoselective and Enantioselective Syntheses of the Four Stereoisomers of Muscol from (3*RS*)-Muscone

by **Yoshifumi Yuasa***[a]), **Haruhiko Fukaya**[b]) and **Yoko Yuasa**[b])

[a]) *Takasago International Corporation*, 13 Sunayama, Kamisu, Ibaraki, 314-0255, Japan (phone: 81-(0)479-46-4801; fax: 81-(0)479-46-3310; e-mail: yoshifumi_yuasa@takasago.com)

[b]) School of Pharmacy, Tokyo University of Pharmacy and Life Science, 1432-1 Horinouchi, Hachioji, Tokyo, 192-0392, Japan (e-mail: fukayah@ps.toyaku.ac.jp; e-mail: yuasay@ps.toyaku.ac.jp)

Two *trans* stereoisomers of 3-methylcyclopentadecanol (= muscol), (1*R*,3*R*)-**2** and (1*S*,3*S*)-**2**, were efficiently synthesized from (3*RS*)-3-methylcyclopentadecanone (= muscone; (3*RS*)-**1**) by a highly stereoselective reduction (*Scheme*). *L-Selectride*® (= lithium tri(*sec*-butyl)borohydride) was used, followed by the enantiomer resolution by lipase QLG (*Alcaligenes* sp.). The *cis* stereoisomers of muscol, (1*S*,3*R*)-**2** and (1*R*,3*S*)-**2**, were obtained by the *Mitsunobu* inversion of (1*R*,3*R*)-**2** and (1*S*,3*S*)-**2**, respectively (*Scheme*). The absolute configuration of (1*R*,3*R*)-**2** was determined by X-ray crystal-structure analysis of its 3-nitrophthalic acid monoester, 2-[(1*R*,3*R*)-3-methylcyclopentadecyl hydrogen benzene-1,2-dicarboxylate ((1*R*,3*R*)-**3b**), and by oxidation of (1*R*,3*R*)-**2** to (3*R*)-muscone.

**Introduction.** – Many reports describe the synthesis of racemic and optically active 3-methylcyclopentadecanone (= muscone; **1**), which is a valuable perfume compound isolated from the male musk deer *Moschus moschiferus* [1][2]. However, little is known about the stereochemically precise synthesis of its reduction product, 3-methylcyclopentadecanol (= muscol; **2**) [3–5][1]. *Mookherjee* and *Trenkle* [6] reported the observation of naturally occurring muscol in a tincture of Tonquin musk; however, the group did not describe the configuration of the compound. The synthesis of (3*R*)-muscol by a lipase-catalyzed resolution has been reported [7][8] although the absolute configuration at the OH-substituted C(1) remains to be described.

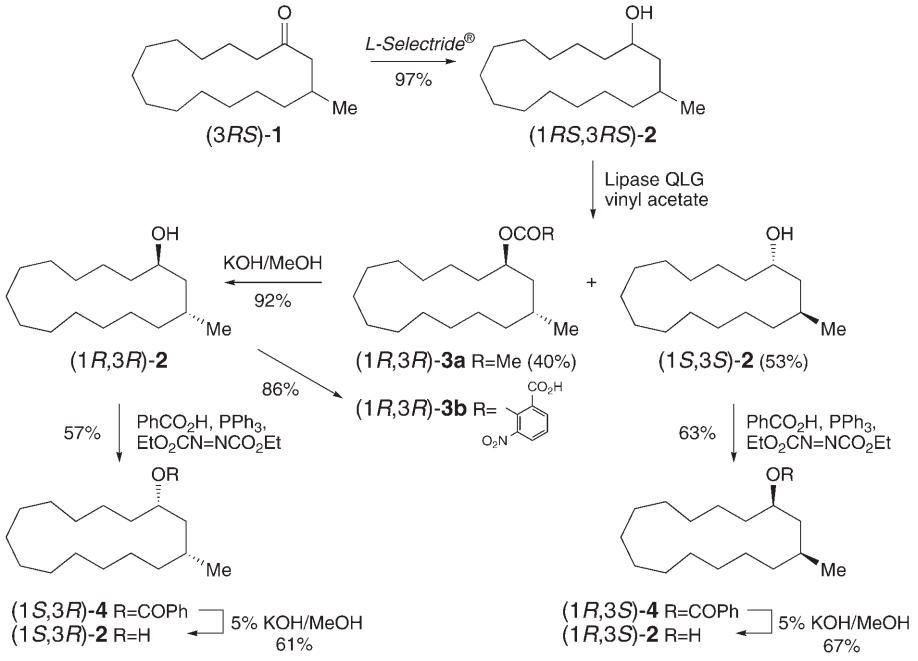
Muscol has four stereoisomers, as shown in the *Scheme*. Two of these, (1*R*,3*R*)-**2** and (1*S*,3*R*)-**2**, are considered to be naturally occurring [6]. Here we report on the syntheses of the four stereoisomers of muscol *via* a three-stage procedure: the stereoselective reduction of muscone ((3*RS*)-**1**) by *L-Selectride*® (= lithium tri(*sec*-butyl)borohydride); the subsequent enantiomer resolution of *trans*-muscol (1*RS*,3*RS*)-**2** by lipase, and, finally, the implementation of the *Mitsunobu* reaction.

**Results and Discussion.** – First, muscone (3*RS*)-**1** was reduced by $NaBH_4$ to give a *trans*/*cis* mixture of muscol (1*RS*,3*RS*)/(1*RS*,3*SR*)-**2** in a 75:25 ratio, as determined by gas chromatography (GC). Initially, the GC peaks were not specifically attributed to the *trans* or *cis* stereoisomers, but peaks were identified after X-ray crystallographic

[1]) Examples for racemic muscol.

analyses. Second, a catalytic hydrogenation of (3*RS*)-**1** over $PtO_2$ was performed to generate (1*RS*,3*RS*)/(1*RS*,3*SR*)-**2**, also in a 75:25 ratio. Next, we attempted to repeat the reduction with *L-Selectride*®, which is known to be highly selective for the *trans* isomer upon reduction of 3-methylcyclohexanone [9]. Thus, (3*RS*)-**1** was reduced with *L-Selectride*® according to the standard protocol at $-78°$ to give a *trans/cis* mixture (1*RS*,3*RS*)/(1*RS*,3*SR*)-**2** with a ratio of 98:2 (*Scheme*). However, the configuration of (1*RS*,3*RS*)-**2** obtained by this highly stereoselective reduction was not determined by measurement of the NOE between H–C(1) and the H–C(3). Enantiomer resolution of (1*RS*,3*RS*)-**2** was achieved by treatment with lipase QLG and vinyl acetate which gave acetate (1*R*,3*R*)-**3a** and alcohol (1*S*,3*S*)-**2**; subsequent hydrolysis of (1*R*,3*R*)-**3a** with 10% KOH in MeOH gave (1*R*,3*R*)-**2** in 92% yield. The enantiomer excess (ee) of (1*R*,3*R*)- and (1*S*,3*S*)-**2**, determined by GC (chiral column *Chirasil DEX-CB*), were 96% and 77%, respectively. For the determination of the absolute configuration by X-ray crystal-structure analysis, (1*R*,3*R*)-**2** was transformed to its 4-nitrophenyl ester and 4-bromophenyl ester; however, these derivatives were not solids in the necessary temperature range. By contrast, 3-nitrophthalic acid monoester (1*R*,3*R*)-**3b**, as derived from (1*R*,3*R*)-**2**, was a solid and therefore suitable for the determination of the relative configuration of (1*R*,3*R*)-**2** by X-ray crystallography (*Fig.*). Furthermore, the absolute configuration was confirmed by measuring the optical-rotation value of (3*R*)-muscone ((3*R*)-**1**) which was obtained from (1*R*,3*R*)-**2** by pyridinium dichromate (PDC) oxidation [8]. Thus, we confirmed the high stereoselectivity of the *L-Selectride*® reduction of (3*RS*)-**1** by generating a 98:2 ratio of the *trans*/*cis*-isomers (1*RS*,3*RS*)/

Scheme. *Syntheses of the Four Stereoisomers of Muscol*



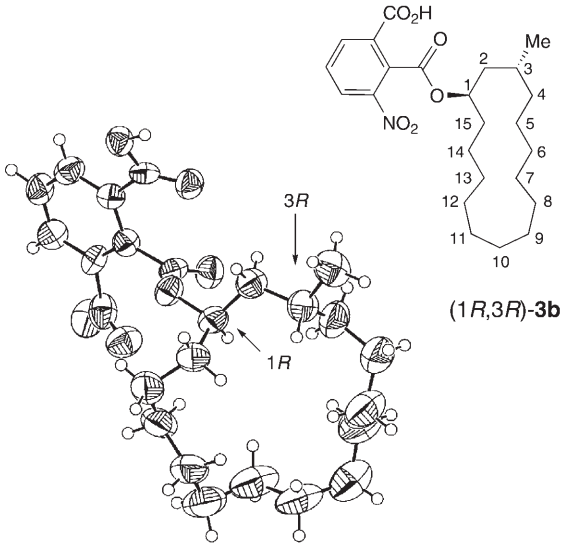



Figure. *X-Ray crystal-structure* (ORTEP plot) *of 2-[(1*R,*3*R*)-3-methylcyclopentadecyl] hydrogen 3-nitrobenzene-1,2-dicarboxylate* ((1*R*,3*R*)-**3b**). Ellipsoids are represented at the 50% probability level.

(1*RS*,3*SR*)-**2**. This result supported the *trans*-selectivity of *L-Selectride*® reduction as, by analogy, described in the literature [9].

Additionally, (1*S*,3*S*)-**2** was determined to be another *trans* isomer of muscol because it was an enantiomer of (1*R*,3*R*)-**2** and was similar to the descriptions in the literature [8]. Moreover, (1*R*,3*R*)- and (1*S*,3*S*)-**2** could be inverted to (1*S*,3*R*)- and (1*R*,3*S*)-**2**, respectively, without racemization by the *Mitsunobu* reaction [10] (*Scheme*), by an inversion reaction at the OH-substituted stereogenic center. The technique described here represents the first successful synthesis of all four stereoisomers of muscol.

## Experimental Part

*General*. All reagents and solvents were obtained from commercial sources and used without further purification. *Lipase QLG* (*Alcaligenes* sp.) was purchased from *Meito Co. Ltd*. CC = Column chromatography. GC: *Shimadzu GC-14A* with an FID detector; carrier gas $N_2$ (0.1 MPa); column *Silicone NB-1* (*df* 0.25 μm, 0.25 mm i.d. × 30 m), with oven temp. 150–250° at 5°/min, injection temp. 250°, and detector temp. 250° ($t_R$ [min] 11.1 ((3*RS*)-**1**), 11.5 ((1*RS*,3*RS*)-**2**; *cis*), 11.7 ((1*RS*,3*RS*)-**2**; *trans*), 9.5 ((1*R*,3*R*)-**3a**)); column *Chirasil DEX-CB* (*df* 0.25 μm, 0.25 mm i.d. × 25 m), with oven temp. 150° (isothermal), injection temp. 230°, and detector temp. 230° ($t_R$ [min] 43.1 ((1*R*,3*R*)-**2**), 39.8 ((1*S*,3*R*)-**2**), 41.0 ((1*S*,3*S*)-**2**), 38.9 ((1*R*,3*S*)-**2**)). M.p.: *Yanagimoto* micro melting apparatus; uncorrected. Optical rotations: *Jasco DIP-4* digital polarimeter. IR Spectra: *Nicolet Avatar-360* FT-IR spectrometer; in $cm^{-1}$. $^1H$- and $^{13}C$-NMR Spectra: *Bruker DRX-500* (500/125 MHz) apparatus; in $CDCl_3$; chemical shifts $\delta$ in ppm rel. to $Me_4Si$ (= 0 ppm) as internal standard, coupling constants *J* in Hz. EI-MS: *Hitachi M-80A* mass spectrometer, at 70 eV; in *m/z* (rel.%).

*X-Ray Crystal-Structure Analysis.* The data describing the crystal structure of (1*R*,3*R*)-**3b** are collected in the *Table,* and a representation of its structure can be found in the *Figure*. All diagrams and

Table. *X-Ray Crystal-Structure Analysis of 2-[(1*R*,3*R*)-3-Methylcyclopentadecyl] Hydrogen 3-Nitrobenzene-1,2-dicarboxylate* ((1*R*,3*R*)-**3b**)

| | | |
|---|---|---|
| Crystallized from | | $Et_2O$/cyclohexane |
| Empirical formula | | $C_{24}H_{35}NO_6$ |
| $M$ [g mol$^{-1}$] | | 433.545 |
| Crystal color, habit | | colorless, prism |
| Crystal dimensions [mm] | | $0.45 \times 0.38 \times 0.25$ |
| Temperature [K] | | 200 |
| Crystal system | | monoclinic |
| Space group | | $P2_1$ |
| $Z$ | | 4 |
| Reflections for cell determination | | 4192 |
| $\theta$ Range for cell determination [°] | | 2.27 – 70.08 |
| Unit-cell parameters: | $a$ [Å] | 6.4150(5) |
| | $b$ [Å] | 38.947(3) |
| | $c$ [Å] | 9.6670(6) |
| | $\alpha$ [°] | 90.00 |
| | $\beta$ [°] | 96.103(4) |
| | $\gamma$ [°] | 90.00 |
| | $V$ [Å$^3$] | 2401.6(3) |
| $D_x$ [g cm$^{-3}$] | | 1.199 |
| $\mu$(Mo$K\alpha$)[mm$^{-1}$] | | 0.70 |
| $\theta_{(max)}$ [°] | | 70.04 |
| Total reflections measured | | 6653 |
| Independent reflections | | 6621 |
| Reflections used ($I > \sigma > (I)$) | | 3.00 |
| Parameters refined | | 556 |
| Final $R$ | | 0.067 |
| $wR$ | | 0.039 |
| Extinction coefficient | | 0.010(2) |
| $\Delta_{max}/\sigma$ | | 0.076 |
| $\Delta/\rho$ (max; min) [e Å$^{-3}$] | | 0.24; −0.29 |

calculations were performed with maXus on a *Bruker Nonius* apparatus (*Delft & MacScience*, Japan). Crystallographic data (excluding structure factors) for the structure of (1*R*,3*R*)-**3b** have been deposited with the *Cambridge Crystallographic Data Center*. CCDC-252031 contains the supplementary crystallographic data for this paper. These data can be obtained, free of charge, *via* www.ccdc.cam.ac.uk/data_request/cif.

*(1*RS,*3*RS*)-3-Methylcyclopentadecanol* (= *Muscol*; (1*RS*,3*RS*)-**2**). (3*RS*)-Muscone (47.68 g, 200 mmol) was dissolved in THF (400 ml) under $N_2$ and cooled to −78° (dry ice/acetone bath). Then, 1M *L-Selectride*® soln. (480 ml, 480 mmol) was added slowly to the mixture. After 5 h at −78°, 30% $H_2O_2$ soln. (226.7 ml, 400 mmol) was added dropwise, and the mixture was warmed to r.t. Next, 5% HCl soln. was added to reach pH 3, and then heptane (2 l). The org. layer was washed with sat. $NaHCO_3$ (1 l) and sat. NaCl soln. (1 l), and dried ($MgSO_4$). The solvent was removed under reduced pressure (0.3 Torr), and the residue was distilled at 130–134°/0.3 Torr: (1*RS*,3*RS*)-**2** (46.6 g, 97%). The *trans* configuration was determined by X-ray crystal-structure analysis (see above).

*Enantiomer Resolution of (1*RS,*3*RS*)-**2**: (1*R*,3*R*)-3-Methylcyclopentadecyl Acetate* ((1*R*,3*R*)-**3a**) *and (1*S,*3*S*)-3-Methylcyclopentadecanol* ((1*S*,3*S*)-**2**). THF (100 ml), vinyl acetate (4.25 g, 49.4 mmol), and (1*RS*,3*RS*)-**2** (24 g, 100 mmol) were added to lipase QLG (12 g, 0.5 mass equiv.). The soln. was stirred at r.t. for 24 h, and the course of the reaction was followed by GC. The product ratio of (1*R*,3*R*)-**3a** to (1*S*,3*S*)-**2** was 49:51. The soln. was filtered, and volatile substances were removed under reduced

pressure to give an oily product (22.77 g). The crude product was separated by CC (silica gel, toluene): (1*R*,3*R*)-**3a** (11.2 g, 40%) and (1*S*,3*S*)-**2** (12.6 g, 53%).

*Data of (1*R,*3*R*)-***3a***: Viscous oil. $[\alpha]_D^{24} = +28.58$ ($c = 1.13$, $CHCl_3$). IR (neat): 2928, 2857, 1735, 1457, 1363, 1243. $^1$H-NMR ($CDCl_3$): 0.92 (*d*, *J* = 6.7, Me); 1.04–1.13 (*m*, 1 H); 1.24–1.60 (*m*, 26 H); 1.64–1.72 (*m*, 1 H); 2.02 (*s*, MeCO); 4.94–5.01 (*m*, H–C(1)). $^{13}$C-NMR ($CDCl_3$): 21.2 (Me); 21.4 (Me); 23.7 ($CH_2$); 25.2 ($CH_2$); 26.5 ($CH_2$); 26.6 (3 $CH_2$); 26.7 ($CH_2$); 26.8 (2 $CH_2$); 27.1 ($CH_2$); 28.5 (CH); 31.8 ($CH_2$); 34.4 ($CH_2$); 41.2 ($CH_2$); 72.5 (CH); 170.7 (CO). EI-MS: 282 (1, $M^+$), 239 (4), 222 (89), 206 (15), 194 (4), 180 (11), 166 (7), 152 (7), 138 (11), 124 (19), 110 (41), 96 (74), 82 (74), 69 (37), 59 (67), 43 (100).

*Data of (1*S,*3*S*)-***2***: trans/cis* 92 : 8 by GC. Optical purity: 77% ee by GC (chiral column). M.p. 36–37°. $[\alpha]_D^{24} = -55.76$ ($c = 1.04$, MeOH). IR ($CHCl_3$): 3684, 3619, 3020, 2930, 2858, 2400, 1521, 1460. $^1$H-NMR ($CDCl_3$): 0.92 (*d*, *J* = 6.7, Me); 0.99–1.08 (*m*, 1 H); 1.25–1.52 (*m*, 27 H); 1.64–1.70 (*m*, 1 H); 3.74–3.79 (*m*, H–C(1)). $^{13}$C-NMR ($CDCl_3$): 21.4 (Me); 23.7 ($CH_2$); 25.2 ($CH_2$); 26.5 ($CH_2$); 26.6 (2 $CH_2$); 26.7 ($CH_2$); 26.8 ($CH_2$); 26.9 ($CH_2$); 27.1 ($CH_2$); 27.4 ($CH_2$); 28.7 (CH); 34.4 ($CH_2$); 34.7 ($CH_2$); 45.4 ($CH_2$); 69.2 (CH). EI-MS: 222 (30, $[M-18]^+$), 196 (19), 180 (4), 166 (4), 152 (4), 138 (8), 124 (15), 110 (30), 96 (70), 82 (13), 71 (100), 57 (30), 43 (22).

*(1*R,*3*R*)-3-Methylcyclopentadecanol* ((1*R*,3*R*)-**2**) *from* (*1*R,*3*R)-**3a**. At r.t., (1*R*,3*R*)-**3a** (10 g, 35.5 mmol) was hydrolyzed by 10% KOH in MeOH for 17 h (100% conversion, by GC). The mixture was concentrated, and 10% aq. AcOH soln. was added for neutralization. The product was extracted with hexane and the extract washed with 5% $NaHCO_3$ soln., dried ($MgSO_4$), and concentrated: (1*R*,3*R*)-**2** (7.84 g, 92%). Ratio *trans/cis* 98 : 2 by GC. Optical purity: 96% ee by GC (chiral column). M.p. 43–44°. $[\alpha]_D^{24} = +69.0$ ($c = 1$, MeOH). Anal. data: identical to those of (1*S*,3*S*)-**2**.

*(1*S,*3*R*)-3-Methylcyclopentadecanol* ((1*S*,3*R*)-**2**) *from (1*R,*3*R*)-**2** by the* Mitsunobu *Reaction.* A 40% diethyl diazenedicarboxylate soln. in toluene (38 ml, 87.4 mmol) was added dropwise to the mixture of (1*R*,3*R*)-**2** (15.0 g, 62.4 mmol), benzoic acid (8.38 g, 68.6 mmol), and triphenylphosphine (19.64 g, 74.9 mmol) in THF (90 ml), under $N_2$ at −15° for 1.5 h. After 4 h at −15°, the insoluble solid was filtered off, and the filtrate was concentrated to give crude benzoate (1*S*,3*R*)-**4** (42.0 g) which was purified by CC (silica gel, toluene): *(1*S,*3*R*)-3-methylcyclopentadecyl benzoate* (1*S*,3*R*)-**4**; 12.3 g, 57%). Viscous oil. $[\alpha]_D^{24} = +0.2$ ($c = 0.5$, $CHCl_3$)[2]. IR (neat): 2980, 2857, 1716, 1451, 1274. $^1$H-NMR ($CDCl_3$): 0.95 (*d*, *J* = 6.7, Me); 1.33–1.49 (*m*, 25 H); 1.57–1.62 (*m*, 1 H); 1.69–1.80 (*m*, 3 H); 5.18–5.23 (*m*, 1 H); 7.26–7.45 (*m*, 2 H); 7.52–7.56 (*m*, 1 H); 8.04–8.05 (*m*, 2 H). $^{13}$C-NMR ($CDCl_3$): 20.7 (Me); 22.9 ($CH_2$); 24.1 ($CH_2$); 26.5 ($CH_2$); 26.6 ($CH_2$); 26.7 (2 CH, $CH_2$); 26.8 ($CH_2$); 27.1 ($CH_2$); 27.4 ($CH_2$); 28.7 (CH); 32.9 ($CH_2$); 35.5 ($CH_2$); 39.9 ($CH_2$); 73.8 (CH); 128.3 (2 CH); 129.5 (2 CH); 131.0 (C); 132.6 (CH); 166.2 (CO). EI-MS: 344 (1, $M^+$), 316 (2), 222 (32), 120 (100), 105 (8), 77 (13), 55 (11), 43 (6).

The benzoate (1*S*,3*R*)-**4** was hydrolyzed by 5% KOH in MeOH at 50° for 5 h. The mixture was concentrated, and 10% aq. AcOH soln. was added for neutralization. The product was extracted with hexane, the extract washed with 5% $NaHCO_3$ soln., dried ($MgSO_4$), and concentrated, and the residue purified by CC (silica gel, AcOEt/hexane 1 : 3): (1*S*,3*R*)-**2** (9.15 g, 61%). Ratio *cis/trans* 98 : 2 by GC. Optical purity: 96% ee by GC (chiral column). M.p. 38–38.5°. $[\alpha]_D^{24} = +11.65$ ($c = 1.0$, MeOH). IR ($CHCl_3$): 3684, 3619, 3021, 2926, 2858, 2400, 1521, 1430. $^1$H-NMR ($CDCl_3$): 0.92 (*d*, *J* = 6.7, Me); 1.17–1.22 (*m*, 1 H); 1.23–1.43 (*m*, 23 H); 1.49–1.58 (*m*, 3 H); 1.59–1.65 (*m*, 1 H); 3.73–3.79 (*m*, H–C(1)). $^{13}$C-NMR ($CDCl_3$): 21.2 (Me); 22.8 ($CH_2$); 23.9 ($CH_2$); 26.6 (2 $CH_2$); 26.7 (2 $CH_2$); 26.8 ($CH_2$); 27.2 ($CH_2$); 27.4 ($CH_2$); 28.8 (CH); 35.5 ($CH_2$); 36.3 ($CH_2$); 43.7 ($CH_2$); 69.8 (CH). EI-MS: 222 (22, $[M^+ - 18]$), 196 (19), 180 (4), 166 (8), 152 (4), 137 (4), 124 (11), 110 (26), 96 (59), 82 (89), 71 (100), 57 (41), 43 (22).

*(1*R,*3*S*)-3-Methylcyclopentadecanol* ((1*R*,3*S*)-**2**) *from (1*S,*3*S*)-**2** by* Mitsunobu *Reaction.* As described for (1*S*,3*R*)-**2**, from (1*S*,3*S*)-**2**: intermediate benzoate (1*R*,3*S*)-**4** (63%) as a viscous oil with $[\alpha]_D^{24} = +0.37$ ($c = 1.02$, $CHCl_3$)[2]) and anal. data identical to those of (1*S*,3*R*)-**4**. Subsequent hydrolysis gave (1*R*,3*S*)-**2** (67%). Ratio *cis/trans* 92 : 8 by GC. Optical purity: 77% ee by GC (chiral column). M.p. 43–44°. $[\alpha]_D^{24} = +3.57$ ($c = 1.0$, MeOH)[2]). Anal. data: identical to those of (1*S*,3*R*)-**2**.

---

[2]) The presence of 8% of another isomer may account for the unexpected identical sense of rotation as compared to the pure enantiomer.

*2-[(1*R,*3*R*)-3-Methylcyclopentadecyl] Hydrogen 3-Nitrobenzene-1,2-dicarboxylate* ((1*R*,3*R*)-**3b**). Isomer (1*R*,3*R*)-**2** (0.5 g, 2.1 mmol) and 3-nitrophthalic anhydride (=4-nitroisobenzofuran-1,3-dione; 0.4 g, 2.1 mmol) were refluxed for 2 h in toluene (30 ml). The solvent was evaporated and the residue purified by CC (silica gel, AcOEt/hexane 1:3): (1*R*,3*R*)-**3b** (0.78 g, 86%). The solid was crystallized from $Et_2O$/cyclohexane. M.p. 135–137°. $[\alpha]_D^{23} = +37.0$ ($c = 0.12$, $CHCl_3$). IR ($CHCl_3$): 2930, 1733, 1700, 1541, 1419, 1352. $^1$H-NMR ($CDCl_3$): 0.95 (*d*, *J* = 6.5, Me); 1.10–1.19 (*m*, 1 H); 1.25–1.68 (*m*, 25 H); 1.78–1.86 (*m*, 1 H); 1.90–1.97 (*m*, 1 H); 5.28–5.32 (*m*, H–C(1)); 7.71 (*t*, *J* = 7.9, 1 arom. H); 8.36–8.40 (*m*, 2 arom. H). $^{13}$C-NMR ($CDCl_3$): 21.1 (Me); 23.5 ($CH_2$); 25.2 ($CH_2$); 26.5 ($CH_2$); 26.6 ($CH_2$); 26.7 (23 $CH_2$); 27.0 ($CH_2$); 27.2 ($CH_2$); 28.5 (CH); 31.4 ($CH_2$); 34.1 ($CH_2$); 40.5 ($CH_2$); 76.6 (CH); 129.1 (C); 129.9 (CH); 132.2 (C); 135.9 (CH); 146.7 (C); 164.3 (CO); 168.3 (CO). EI-MS: 433 (1, $M^+$), 372 (1), 279 (1), 239 (2), 223 (11), 222 (25), 196 (7), 195 (20), 194 (66), 177 (18), 166 (6), 152 (9), 150 (13), 123 (14), 122 (14), 110 (23), 109 (22), 96 (62), 95 (55), 81 (100), 67 (89).

*(3*R*)-3-Methylcyclopentadecanone* ((3*R*)-**1**) *from (1*R,*3*R*)-**2**. To a soln. of (1*R*,3*R*)-**2** (0.5 g, 202 mmol) in $CH_2Cl_2$ (30 ml), PDC (1.9 g, 505 mmol) was added. The mixture was stirred vigorously at r.t. for 48 h and then filtered through *Celite*. The filtrate was concentrated and the residue purified by CC (silica gel, AcOEt/hexane 1:20): (3*R*)-**1** (0.39 g, 81%). $[\alpha]_D^{23} = -12.6$ ($c = 1.0$, MeOH) [8]: $[\alpha]_D^{23} = -12.7$ ($c = 1.0$, MeOH). NMR: identical with those of [8].

## REFERENCES

[1] H. Walbum, *J. Prakt. Chem*. **1906**, *73*, 488.
[2] L. Ruzicka, *Helv. Chim. Acta* **1926**, *9*, 715.
[3] M. Baumann, W. Hoffmann, N. Mueller, *Tetrahedron Lett*. **1976**, 3585.
[4] W. G. Robert, A. S. Dreiding, *Helv. Chim. Acta* **1997**, *60*, 1969.
[5] K. A. Nelson, E. A. Mash, *J. Org. Chem.* **1986**, *51*, 2721.
[6] B. D. Mookherjee, R. W. Trenkle, '8th International Congress of Essential Oils', Cannes, France, Abstracts, 1980, p. 580–583.
[7] K. Takabe, T. Aoyama, Y. Yamada, H. Tada, '39th Symposium on the Chemistry of Terpene, Essential Oils, and Aromatics', 1995, Abstracts 1 III 1l, p. 177–178.
[8] Y. Matsumura, H. Fukawa, Y. Terao, *Chem. Pharm. Bull.* **1998**, *46*, 1484.
[9] H. C. Brown, S. Krishnamurthy, *J. Am. Chem. Soc*. **1972**, *94*, 7159.
[10] D. L. Hughes, *Org. React.* **1992**, *42*, 355.

*Received December 15, 2006*